

# Overview of Common Causes of Chronic Cough

## ACCP Evidence-Based Clinical Practice Guidelines

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**Objective:** To review the literature on the most common causes of chronic cough.

**Methods:** MEDLINE was searched (through May 2004) for studies published in the English language since 1980 on human subjects using the medical subject heading terms “cough,” “causes of cough,” and “etiology of cough.” Case series and prospective descriptive clinical trials were selected for review. Also obtained were any references from these studies that were pertinent to the topic

**Results:** Upper airway cough syndrome (UACS) due to a variety of rhinosinus conditions, previously referred to as *postnasal drip syndrome*, asthma, nonasthmatic eosinophilic bronchitis (NAEB), and gastroesophageal reflux disease (GERD) are the most common causes of chronic cough. Each of these diagnoses may be present alone or in combination and may be clinically silent apart from the cough itself.

**Conclusion:** In the absence of evidence for the presence of another disorder, an approach focused on detecting the presence of UACS, asthma, NAEB, or GERD, alone or in combination, is likely to have a far higher yield than routinely searching for relatively uncommon or obscure diagnoses.

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**Key words:** asthma; chronic cough; gastroesophageal reflux; nonasthmatic eosinophilic bronchitis; postnasal drip syndrome; upper airway cough syndrome

**Abbreviations:** ACE = angiotensin-converting enzyme; GERD = gastroesophageal reflux disease; NAEB = nonasthmatic eosinophilic bronchitis; PNDS = postnasal drip syndrome; UACS = upper airway cough syndrome

During the past 25 years, the foundation for clinical research into the question of what are the most common causes of chronic cough has been based on a hypothesis set forth in a comprehensive review article published in 1977.<sup>1</sup> In that publication, it was postulated that because there were a relatively small number of known anatomic locations for afferent cough receptors and nerves that it logically followed that there were a definable number of diseases or conditions that could stimulate these sites and result in chronic or persistent cough. The subsequent findings from various descriptive studies in the literature that have looked at populations of patients seeking medical attention for a primary

complaint of cough have in fact corroborated this spectrum of conditions as initially postulated. This body of literature has also defined the relative frequency with which these etiologies of cough occur, the typical manifestations, the value of various diagnostic tests, and the likely responses to treatment. A summary of the main studies is presented in Table 1. Supplementing these studies have been reports that have focused on the specific mechanisms, manifestations, and response to treatment for each of the specific causes of cough delineated in the broader studies. In preparing this section, MEDLINE was searched (through May 2004) for studies published in the English language since 1980 on human subjects using the medical subject heading terms “cough,” “causes of cough,” and “etiology of cough.” Case series and prospective descriptive clinical trials were selected for review. Also, any references from these studies that were pertinent to the topic were obtained.

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**Table 1—Summary of Studies of Common Causes of Cough Reported in the Literature\***

Study/Year	Patients, No.	Country	PNDS/BA/GERD,† %	EB,%	PI,%	CB (COPD)	Misc or No Dx
Irwin et al <sup>2</sup> /1981	49	US	82	0	0	12	6
Poe et al <sup>18</sup> /1982	109	US	44	0	25	12	19
Puolijoki and Lahdensuo <sup>19</sup> /1989	198	Finland	34	0	15	4	47
Irwin et al <sup>3</sup> /1990	102	US	86	0	0	5	9
Pratter et al <sup>4</sup> /1993	45	US	96	0	0	0	4
O'Connell et al <sup>21</sup> /1994	87	Ireland	40	0	10	0	49
Mello et al <sup>6</sup> /1996	88	US	92	0	0	0	8
McGarvey et al <sup>20</sup> /1998	43	Ireland	81	0	0	0	19
Brightling et al <sup>13</sup> /1999	91	UK	47	13	13	7	20
Palombini et al <sup>7</sup> /1999	78	Brazil	94	0	0	0	6
Ayik et al <sup>14</sup> /2003	39	Turkey	44	31	5	0	20

\*BA = bronchial asthma; CB = chronic bronchitis; EB = eosinophilic bronchitis; PI = postinfectious; Misc = miscellaneous; Dx = diagnosis.

†One, two, or all three diagnoses are present.

The composite picture has been remarkably consistent. In a relatively small subset of patients with chronic cough who were seeking medical attention,<sup>2–4</sup> either current cigarette smoking or the use of an angiotensin-converting enzyme (ACE) inhibitor have proven to be the cause of the cough. In the vast majority of the remaining patients, the following three dominant etiologies have emerged to explain the causes of chronic cough: upper airway cough syndrome (UACS) due to a variety of rhinosinus conditions, which was previously referred to as postnasal drip syndrome (PNDS); asthma; and gastroesophageal reflux disease (GERD).<sup>2–6</sup> In four prospective studies<sup>2,6,7,10</sup> from the Western Hemisphere, this triad of diagnoses was so ubiquitous that in 92 to 100% of patients who were nonsmokers, and who were not using an ACE inhibitor, and who had normal chest roentgenogram findings, the presence of one, two, or even all three of these conditions proved to be the etiologic explanation for chronic cough. Even in areas where tuberculosis is endemic, and was an important consideration as a cause of chronic cough, UACS, asthma, nonasthmatic eosinophilic bronchitis (NAEB), and GERD are still the most common causes seen.

It is important to recognize, as will be discussed under each individual section, that each of these entities may present only as cough with no other associated clinical findings (*ie*, “silent PNDS” [now termed UACS], “cough variant asthma,” and “silent GERD”).<sup>4,8,9</sup> It is also important to note that the medical history is of little value as regards the patient’s description of his or her cough in terms of its character or timing, or the presence or absence of sputum production. None of these characteristics is of diagnostic value.<sup>6,10</sup> Even in the presence of significant bronchorrhea, a nonsmoking patient who is not receiving an ACE inhibitor and who has a normal chest roentgenogram finding will usually turn

out to be coughing due to UACS, asthma, GERD, or some combination of these diagnoses.<sup>10</sup> Nevertheless, the medical history is important in terms of whether the patient is taking an ACE inhibitor, is or has been a smoker, or lives or has been in a geographic area where tuberculosis or certain fungal diseases are endemic. In addition, the medical history is important as to whether there is any previous history of cancer, tuberculosis, or AIDS, or whether the patient has any systemic symptoms of fever, sweats, or weight loss.

It is still important to recognize, however, that there are a number of other conditions, although much less common on average, that still account for an important percentage of cases of chronic cough. For example, NAEB, which is a disorder that is characterized by cough, eosinophilic infiltration of the bronchial tree, normal spirometry findings, a lack of bronchial hyperresponsiveness, and a resolution of both cough and eosinophilia with steroid treatment,<sup>11–14</sup> has been reported to have a prevalence as an etiology of chronic cough from as low as 13% to as high as 33% in a number of series from outside the United States.<sup>7,14,19–21</sup> Oddly, a number of large studies<sup>2–5</sup> of chronic cough in the United States to date have been able to define the etiology in up to 100% of cases without reporting a single diagnosis of NAEB. Nevertheless, a diagnosis of NAEB should be considered early in the diagnostic evaluation in that its presence can be reliably determined by properly performed staining of induced sputum for eosinophils, and by the fact that it will predictably respond to (inhaled) corticosteroid therapy.

Whereas one series<sup>5</sup> of patients with chronic cough (performed in the United States) described a significant number of patients with “postinfectious” cough, other series<sup>2,4–7</sup> were able to reach a high diagnostic yield without using this category. The implication is that most of the cases of postinfectious

cough had as their pathophysiology persistent UACS, transient bronchial hyperresponsiveness, or prolonged airway inflammation that resolved as diagnostic/therapeutic studies were being pursued. A subset of "postinfectious cough," due to *Bordetella pertussis*, is another entity that has not been described at all in many series of patients<sup>15–17</sup> with chronic cough, but which may be etiologic in a localized cluster of patients with chronic cough as part of a localized epidemic. Or, it may be pathophysiologically involved in perpetuating chronic cough by provoking GER. Patients with bronchiectasis from a variety of causes, such as interstitial lung diseases, endobronchial abnormalities (eg, tumors, tuberculosis, sarcoidosis, or retained sutures), isolated suppurative lower airway infection, congestive heart failure, thyroid disease, habitual or psychogenic cough, neuromuscular disorders, or a mediastinal mass, will occasionally present with chronic cough as the major manifestation.

In summary, the most common causes of chronic cough are UACS due to a variety of rhinosinus conditions, asthma, and GERD. Each of these diagnoses may be present alone or in combination and may be clinically silent apart from the cough itself. While there are a number of other conditions that can result in chronic cough, in the absence of evidence suggesting the presence of one of these other disorders, an approach strongly focused on initially detecting the presence of UACS, asthma, or GERD, alone or in combination, is likely to have a far higher yield than routinely searching for relatively uncommon or obscure diagnoses. The one exception to this is that NAEB may be more important than has often been recognized, is relatively easy to diagnose in laboratories set up to do the rigorous analysis and treatment, and therefore should also be considered early in the diagnostic evaluation.

#### SUMMARY OF RECOMMENDATIONS

**1. In patients with chronic cough and a normal chest roentgenogram finding who are nonsmokers and are not receiving therapy with an ACE inhibitor, the diagnostic approach should focus on the detection and treatment of UACS (formerly called PNDS), asthma, NAEB, or GERD, alone or in combination. This approach is most likely to result in a high rate of success in achieving cough resolution.** Level of evidence, low; benefit, substantial; grade of recommendation, B

**2. In all patients with chronic cough, regardless of clinical signs or symptoms, because UACS (formerly called PNDS),**

**asthma, and GERD each may present only as cough with no other associated clinical findings (ie, "silent PNDS," "cough variant asthma," and "silent GERD"), each of these diagnoses must be considered.** Level of evidence, low; benefit, substantial; grade of recommendation, B

**3. In patients with chronic cough, neither the patient's description of his or her cough in terms of its character or timing, nor the presence or absence of sputum production, should be used to rule in or rule out a diagnosis or to determine the clinical approach.** Level of evidence, low; benefit, substantial; grade of recommendation, B

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